Synthesis of Novel 2,3-Diarylquinoline Derivatives as Antiproliferative Agents

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A number of 2,3-diarylquinoline derivatives were synthesized and evaluated for antiproliferative activities against the growth of six cancer cell lines including human hepatocelluar carcinoma (Hep G2 and Hep 3B), non-small cell lung cancer (A549 and H1299), and breast cancer (MCF-7 and MDA-MB-231) cell lines. The preliminary results indicated that 6-fluoro-2,3-bis{4-[2-(piperidin-1-yl)-ethoxy]phenyl}quinoline **(16b)** was more active than Tamoxifene against the growth of Hep 3B, H1299, and MDA-MB-231 with GI_{50} values of 0.71, 1.46, and 0.72 M respectively. Further investigations have shown that **16b** induce cell cycle arrest at G2/M phase in a concentration- and time- dependent manner, DNA fragmentation, and disrupt the microtubule network in MDA-MB-231 cells. The apoptotic induction was related to increase in the protein expressions of Bad and Bax and decrease in Bcl-2.